PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2006/002350	26.06.2006	28.06.2005

International Patent Classification (IPC) or both national classification and IPC
INV. C07K14/775 A61K38/04

Applicant
AI2 LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Chavanne, Franz Telephone No. +49 89 2399-8399

Form (PCT/ISA/237) (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2006/002350

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☒ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☒ on paper

      ☒ in electronic form

   c. time of filing/furnishing:

      ☒ contained in the international application as filed.

      ☒ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 21, 22

because:

☒ the said international application, or the said claims Nos. 21, 22 relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4, 8, 9, 12, 16-20, 22-24
	No:	Claims	1-3, 5-7, 10, 11, 13-15, 21
Inventive step (IS)	Yes:	Claims	4, 8, 9, 12, 16, 22-24
	No:	Claims	1-3, 5-7, 10, 11, 13-15, 17-21
Industrial applicability (IA)	Yes:	Claims	1-20, 23, 24
	No:	Claims	

2. Citations and explanations

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 21 and 22 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 02/15923
   D2: WO 2005/039534

2. D1 describes polypeptides which are used for the treatment of fungal infections leading to cardiovascular complications. These polypeptides comprise peptides comprising repeats of short peptide sequences of the peptides of SEQ ID No.5-7, such as e.g. repeats of the dimers L-K, F-F, K-F, etc... Moreover, the polypeptides of D1 may be composed of multimeric combinations of said peptides. Hence, fragment of the peptides of D1 which are comprised in the peptides of SEQ ID No.5-7 of the present application would be repeated in the resulting polypeptide (abstract; paragraphs 11, 70, 71, 85; claim 80).
   Thus, in view of D1, the subject-matter of claims 1-3, 5-7, 10, 11, 13-15 and 21 is not novel (Article 33(2) PCT).
   In this context, the Applicant shall be aware that "a derivative" of a specific sequence can result in any other sequence after having applied the appropriate deletions, insertions and/or substitutions. The same applies to "a variant" of a specific peptide.

3. D2 describes particles comprising one or several lipid binding polypeptides and one or more bioactive agent. The lipid binding polypeptide can be the apolipoprotein E (ApoE) or apolipoprotein B (ApoB) LDL receptor binding domain, the bioactive agent can be an agent having anti-fungal (AmB) or anti-protist (anti-Leishmania) activities.

Hence, D2 describes a particle which is a "derivative" or "analogue" of a polypeptide. This "derivative" comprises several ApoE or ApoB LDL receptor binding domains, and thus, is composed of repeats of ApoE or ApoB LDL receptor binding domains. Moreover, this derivative has an anti-fungal or anti-protist activity through the presence of the bioactive agent.
Thus, in view of D2, the subject-matter of claims 1-3, 5-7, 10, 11, 14 and 21 is not novel (Article 33(2) PCT.

4. D2 does not specifically refers to the treatment or prevention of the specific strains mentioned in claims 17-20. However, bioactive agents against these strains are known in the art. Thus, the subject-matter of claims 17-20 corresponds to obvious alternatives to the teachings of D2 (Article 33(3) PCT).

5. Claims 1, 5, 10, 15 and 21 lack clarity due to the terms "derivative", "analogue" and "variant". These terms are vague, unclear, subject to individual interpretation, and thus, not adapted to clearly define the scope of the claims (see above) (Article 6 PCT). The same applies to the term "derived" in claims 1-3, 13 and 14 (Article 6 PCT).

6. The claims are defined in such a way that their scope encompasses subject-matter which does not solve the technical problem. In fact, the present application shows that apolipoproteins do not provide any anti-fungal or anti-protist activity. Hence, it is very unlikely that fusion proteins comprising two apolipoproteins would have the required anti-fungal and/or anti-protist activity. However, such a fusion protein would comprise repeats of a peptide derived from a Heparan Sulphate Proteoglycan receptor binding region of an apolipoprotein. Hence, the present application is not enabling **over the whole scope** of the claims (Article 5 PCT).